REMARKS

Status of the Claims

Claims 2 to 5, 7 to 13, 18, 22 to 24, 26, 27, and 34 to 38 were acted upon by the Examiner in the Office Action, dated June 13, 2006. Claims 18 and 34 to 38 have been amended. No claims have been canceled. Claim 39 has been added. Accordingly, claims 3 to 5, 7 to 13, 18, 22 to 24, 26, 27, and 34 to 39 are presented for examination.

Summary of the Applicant's Invention

Before discussing the Examiner's rejection in detail applicants believe it would be helpful to explain the basis of the present invention and why this invention is particularly important to availability, transportation, and maintenance of viral vectors/particles. Basically, applicants have discovered a method for enhancing the titer of or preserving recombinant adenovirus vectors or particles. The methods of the invention utilize specific compositions or solutions that maintain or enhance the titer of the vectors or particles at temperatures above freezing for long periods of time (greater than 3 months). The benefits of such a method are readily apparent to those of skill in the art. In particular, repetition of the freeze-thaw cycle can destroy the integrity of cells, proteins, and nucleic acids. The methods of the present invention enable a scientist to use the same viral stock while minimizing the number of freeze-thaw cycles. Minimization of the number of freeze-thaw cycles helps maintain a more consistent viral titer, which is important in nearly all uses of a viral vector system. In addition, maintaining the virus at a temperature above freezing (i.e., in a liquid state) leaves the virus in a state that is more readily available, easily transported, and economically maintained. Such methods may be particularly important when viral vectors/particles need to be provided to scientists or physicians in areas with limited ability to transport or store the vectors/particles in a frozen state prior to experimentation or medical use.

Summary of the Examiner's Action

Claim Rejections

Claims 3 to 5, 7 to 13, 18, 22 to 24, 26, 27, and 34 to 38 stand rejected under 35 U.S.C. §112, first paragraph (written description).

Claims 7 to 13, 22 to 24, 26, and 34 to 38 stand rejected under 35 U.S.C. §103(a), as being unpatentable over Crespo (WO 97/33975, wherein the English version is US 6,248,588) in view of Engler (US 2003/0211598).

Claims 3 to 5, 7 to 13, 18, 22 to 24, 26, 27 and 34 to 38 stand rejected under 35 U.S.C. §103(a), as being unpatentable over Crespo taken with Engler and further in view of Rolland (US 6,040,295) or Sene (WO 98/02522, wherein its English version is US 6,451,256).

Applicants respectfully traverse the Examiner's rejection.

Discussion

Amendments to the Claims

Claim 34 has been amended to recite a composition "consisting essentially of" and to further define the storage temperature and length of storage. Support for these amendments is found in Example 6 (page 33, line 29 to page 36, line 13) and Figure 11 of the application.

Claims 18 and 35 to 38 formerly depended from claim 34. These claims have been re-written as independent claims.

Support for new claim 39 is found in table 4 (page 26) of the application.

The 35 U.S.C. §112, First Paragraph, Rejections

Claims 3 to 5, 7 to 13, 18, 22 to 24, 26, 27, and 34 to 38 stand rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. In particular, the Examiner asserts that the specification lacks support for all temperatures above 4°C and all storage periods over 3 months. Claims 18 and 34 to 38 have all been amended to recite "a temperature from about 4°C to about 20°C for at least 3 months to about 8.5 months". Support for this time period is found in Example 6 (page 33, line 29 to page 36, line 13) and Figure 11 of the application. A review of these sections of the application makes it clear that applicants were in possession of the method that is to be used over these temperature ranges and time periods.

Accordingly, Applicants respectfully request that the rejection of claims 3 to 5, 7 to 13, 18, 22 to 24, 26, 27, and 34 to 38 under 35 U.S.C. §112, first paragraph (written description), be withdrawn.

The 35 U.S.C. §103(a) Rejections

Claims 7 to 13, 22 to 24, 26, and 34 to 38 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Crespo in view of Engler et al. Applicants respectfully traverse the rejection.

Applicants submit that they the claims submitted in the reply, dated March 15, 2006, are patentable over the combination of Crespo and Engler et al. for the reasons of record. Crespo does not disclose compositions useful for preserving adenovirus at temperatures in the claimed range for the claimed time period and there is no evidence to suggest that the compositions of Crespo would be effective at these temperatures. In contrast, the presently claimed invention is effective at temperatures from about 4°C to about 20°C.

The present amendments have been provided in order to move prosecution forward as applicants maintain their previous assertions that the previous obviousness rejections are deficient.

With regard to a *prima facie* obviousness rejection, MPEP §2143 states:

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.
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> The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in Applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Accordingly, a proper *prima facie* case of obviousness requires that the combination teach all of the claim limitations. Applicants submit that the present rejection has not satisfied this requirement.

Presently amended claim 34, from which claims 7 to 13, 22 to 24, and 26 all depend directly or indirectly, recites (emphasis added):

A method of enhancing the titer of or preserving recombinant adenovirus vectors or particles comprising:

a) preparing a purified sample of said recombinant adenovirus vectors or particles;

b) mixing said sample with a composition ***consisting essentially of*** human serum albumin (HSA), wherein the concentration of HSA is from about 0.01% to about 25% (w/v), wherein the pH of said composition is greater than or equal to 5.0 and less than or equal to 9.0; and

c) storing said recombinant adenovirus vectors or particles at a temperature from about 4°C to about 20°C for at least 3 months to about 8.5 months.

Applicants submit that neither Crespo nor Engler et al. disclose a composition ***consisting essentially of*** human serum albumin (HSA), wherein the concentration of HSA is from about 0.01% to about 25% (w/v), wherein the pH of said composition is greater than or equal to 5.0 and less than or equal to 9.0.

The solutions of Crespo all require a gelatin solution (see column 2, line 64, to column 3, line 62). In contrast, claim 34 does not require gelatin. Engler et al., which relates to delivery-enhancing agents and has been cited for the teaching of a Tris-HCl buffer, provides no basis to remove the gelatin from the solutions of Crespo. Accordingly, the combination of Crespo nor Engler et al. does not disclose the compositions of presently amended claim 34.

Claims 18 and 35 to 38 all require compositions that contain the same elements as the composition of claim 34, except that they also consist essentially of other elements. As the combination of Crespo and Engler et al. does not disclose the composition of claim 34, the combination also does not disclose the composition of claims 18 and 35 to 38.

Accordingly, Applicants respectfully request that the rejection of claims 7 to 13, 22 to 24, 26, and 34 to 38 under 35 U.S.C. §103(a) as being unpatentable over Crespo in view of Engler et al. be withdrawn.

Claims 3 to 5, 7 to 13, 18, 22 to 24, 26, 27 and 34 to 38 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Crespo taken with Engler et al. and further in view of Rolland et al. (US 6,040,295) and Sene (WO 98/02522, wherein the English version is US 6,451,256).

Applicants respectfully traverse the rejection.

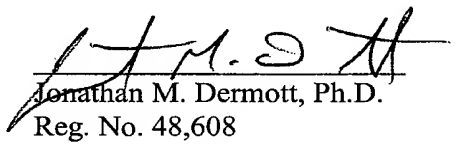
Rolland et al. discloses compositions and methods for enhancing the uptake of nucleic acids by cells or organisms and has been cited for its teaching of an isotonic solution comprising 150 mM NaCl. Sene discloses methods for preserving viral particles in a sucrose solution and has been cited for its teaching of Tris-HCl buffer with pH between 8 and 9.

For the reasons noted above, claims 7 to 13, 22 to 24, 26, and 34 to 38 are non-obvious in view of the combination of Crespo and Engler et al. Rolland et al. and Sene provide no basis to overcome the deficiencies of this combination. In addition, the Examiner has provided no basis for why one of skill in the art would combine Rolland et al., which discloses compositions and methods for enhancing the uptake of nucleic acids by cells or organisms, with Crespo, which is directed to compositions and methods for the preservation of cells and virus particles. Thus, there is no motivation to combine Rolland et al. with Crespo. Accordingly, it appears as if the motivation to add an isotonic solution comprising 150 mM NaCl to the teaching Crespo is based on a hindsight reconstruction of applicants' invention.

Accordingly, Applicants respectfully request that the rejection of claims 3 to 5, 7 to 13, 18, 22 to 24, 26, 27 and 34 to 38 under 35 U.S.C. §103(a) as being unpatentable over Crespo taken with Engler et al. and further in view of Rolland et al. and Sene be withdrawn.

A favorable action on the merits is requested respectfully.

Respectfully submitted,



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